

ble clinically. This is an important period. We may suspect oncoming jaundice from the clinical history, and usually corroborate it with the laboratory procedure known as the icterus index test. This requires time and demands the use of a colorimeter.

The test to which I wish to call attention is instantaneous, accurate, and calls only for equipment usually found in the physician's office. Description of it first appeared in the German literature ten years ago, but was promptly forgotten. The test consists of the intracutaneous injection of 0.10 cubic centimeters of 1 to 1000 solution of histamin in the form of a wheal on the flexor surface of the forearm. In the normal patient with an icterus index below 10, this wheal will remain colorless. In the patient with latent or actual jaundice, it will rapidly become yellow. The test is accurate, and its only contraindication lies in the possibility of its being given to patients who may be sensitive to histamin. The small dosage and low dilution, however, should preclude serious reactions.

This is a valuable procedure, and one that will be of considerable import in judging prognosis, formulating diagnosis, and advising appropriate treatment of the patient with early, subicteric jaundice.

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Fan in Bedroom Need Not Endanger the Health If Properly Used.—An electric fan in the bedroom need not endanger the health if proper attention is given to the type of machine and its location, W. E. Carson, M. D., Pittsburgh, advises in *Hygeia, The Health Magazine*.

For comfort on hot nights without fear of inducing colds, neuritis or rheumatic symptoms, Doctor Carson points out, the fan should not blow directly on the occupants of the room. It should not produce a noticeable breeze but rather a gentle, continuous circular current of air around the room. "The ideal arrangement for a small or medium sized room," he says, "is to have the fan on the wall slightly above the heads of the occupants, so placed that the air current will be directed at an angle to cause it to impinge successively on the different walls in the room. For larger rooms, two fans may be used."

Other satisfactory positions for the fan are on a table near the bed and on the floor at the side of the bed. In both instances the fan should be turned to blow away from the bed.

"A fan giving a direct or continuous air current is to be preferred to the oscillating type," Doctor Carson recommends. "It is self-evident that a fan does not *cool* the air but acts to give comfort only by preventing the accumulation of a stagnant or dead layer of air around the individual. For this purpose a gentle *continuous* current of air is more effective than the intermittent puffs of an oscillating fan. Moreover, the former type is less expensive than the oscillating type, is simpler in construction and is more easily kept in working order. The oscillating fan is preferable only when it is desired to keep flies or other insects from lighting on foodstuffs."

Efforts to eradicate tuberculosis should not be spread thin like butter over bread.—Louis I. Dublin, M. D., Metropolitan Life Insurance Company.

ORIGINAL ARTICLES

THE INTERPRETATION OF LABORATORY EXAMINATIONS IN THE DIAGNOSIS OF INFECTIOUS DISEASES*

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PART I

IN the diagnosis of infectious diseases, the physician relies mainly upon the clinical features and the course of the disease, together with the laboratory examinations. Indeed, there is no field of medicine in which the correct interpretation of laboratory examinations yields greater information than in the infectious diseases. Every few years new diagnostic tests are recommended and, in order that we may obtain the maximum assistance and at the same time appreciate the limitations of such tests, it is well to review in a critical manner a number in common use. Today I propose summarizing some of the practical interpretations of laboratory methods, when applied to the diagnosis of infectious diseases, as illustrated by cases which have come under my own observation.

THE SIGNIFICANCE OF BACTEREMIA

A very common problem in medical diagnosis is the determination of the cause of fever without localizing signs. A frequent examination in this situation is to culture the blood for organisms. The cultures should be incubated in an atmosphere of 10 per cent CO₂, as well as aerobically, since in this way some organisms will grow which would fail to do so if only one method were used. This is particularly true of *Br. abortus*, the gonococcus and meningococcus. The common contaminating organisms, in our experience, are staphylococci and diphtheroids; less often colon bacilli and nonhemolytic streptococci. When staphylococci, colon bacilli, or nonhemolytic streptococci are found in the circulating blood, their significance must be interpreted in the light of the clinical picture and the nature of the primary infection. The presence of micro-organisms in the blood is diagnostic for certain infections, but in others it yields information that is of greater significance in prognosis. This is especially true in pneumococcal, streptococcal and staphylococcus infections, in which the fatality rate without special forms of treatment is between 70 and 98 per cent. For this reason it is of great importance to culture the blood in all cases of these infections, in order that information of prognostic value may be obtained.

Speaking broadly, bacteremia is due to a temporary loss of equilibrium between the normal clearing mechanism of the blood and tissues, and the local defense mechanism at the site of the primary infection, or it may mean that there is an intravascular focus of infection, such as a thrombophlebitis or

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Read before the General Medicine Section of the California Medical Association at the sixty-eighth annual session, Del Monte, May 1-4, 1939.

endocarditis. The interpretation of bacteremia must depend upon the circumstances in which it is observed.

A few diagnostic points in the interpretation of blood cultures may be outlined as follows:

The presence of bacteremia in a patient with mastoiditis should immediately raise the question of a complicating lateral sinus thrombosis, just as bacteremia following tonsillitis suggests thrombophlebitis of the tonsillar veins.

The finding of colon bacilli in the blood, in an individual with pyelonephritis who has not been cystoscoped, catheterized or operated on, should suggest thrombophlebitis of the renal or interlobular veins of the kidney. Colon bacillus bacteremia without signs of pyelonephritis usually means an infection of the gall-bladder or biliary passages.

Staphylococcus aureus bacteremia, without localizing signs of infection, usually indicates an infective endocarditis or an osteomyelitis which has failed to produce localized symptoms. Occasionally—and this is true in about 10 per cent of the cases—there is no obvious portal of entry, and the course is so rapid that no focal abscesses are ever found. Other local foci of infection may be found in the prostate or the muscles.

Pneumococcus bacteremia without pneumonia suggests (1) osteomyelitis, especially in children; (2) paranasal sinus disease; (3) pneumococcus infection of the peritoneum or biliary passages, especially in patients with cirrhosis of the liver, or lipid nephrosis, and (4) pneumococcus endocarditis.

Hemolytic streptococcal bacteremia, without obvious local signs of infection, should suggest thrombophlebitis of the pelvic veins, the tonsillar veins or the veins of the skull; rarely thrombophlebitis of the axillary or pulmonary veins. Following pneumococcus pneumonia, hemolytic streptococcal infection with bacteremia may be observed. It indicates a superinfection of the lung or an infection of the middle ear and mastoid cells. In rare cases it may be a sign of a peritonitis.

It is generally assumed that the presence of typhoid or paratyphoid bacilli in the blood is sufficient for the diagnosis of enteric fever, in the sense that the primary focus is in the gastro-intestinal tract. On occasions, however, it may indicate that one is dealing with a focus of infection elsewhere which is responsible for the bacteremia, and the recognition of such a focus may assist in treatment. As a rule, such foci of infection are found in the gall-bladder, the spleen or the kidneys.

The following cases illustrate the importance of blood cultures in the diagnosis of infections as well as the difficulty in their interpretation.

REPORT OF CASES

A young man with high fever, leukocytosis, and pneumonia shows pneumococcus Type XVIII and B. paratyphosus B in the sputum, and B. paratyphosus B in the blood. His clinical course was that of pneumonia and enteric fever.

CASE 1.—A young man, 18 years of age, entered the hospital complaining of sharp pain in the chest of one day's duration. He was well until five days before admission

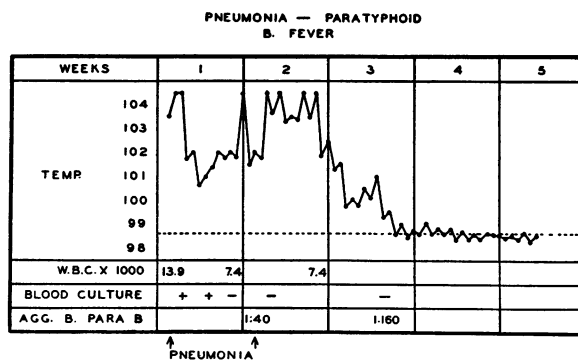


Fig. 1.—(Case 1) Chart showing clinical course of patient with pneumonia and paratyphoid B fever. The etiologic diagnosis was made on the basis of the blood culture.

when he developed fever, the constitutional symptoms of an infection, and a slight cough which became severe within several days and was productive of blood-tinged sputum. On the fourth day of his illness he was drowsy and apathetic and complained of a sharp pain in the left side of the chest which was aggravated by cough and respiratory effort.

The examination showed a young man who was mentally clear in spite of high fever. The respiratory rate was accelerated and there were signs of pneumonia at the base of the left lung posteriorly. The abdomen was not distended and the spleen was not palpable. The leukocyte count was 13,900 per cubic millimeter, the x-ray of the chest showed solidification of the left lower lobe. The blood culture was positive for *B. paratyphosus B*, and the sputum contained the same organism and a pneumococcus Type XVIII.

The course of the disease is shown in Fig. 1.

This case illustrates the importance of the blood culture in the diagnosis of a pulmonary infection, and its considerable importance in view of the fact that the same organism was found in the sputum along with a Type XVIII pneumococcus. Later in the course of the disease, the agglutination reaction became positive for *B. paratyphosus B*, but the patient never developed any agglutinins against the pneumococcus Type XVIII. Without the blood culture, this case might very well have been diagnosed as an atypical pneumonia due to Type XVIII pneumococcus. From the laboratory examination one was able to establish the diagnosis of paratyphoid infection of the lung and blood.

This case was not unlike many that have been described in the past by a number of authors as "Pneumotypoid," and Bullowa¹ and Klein and Torrey² have described cases of *B. paratyphosus pneumonia*. It is well to recall that, of the metastatic infections of *B. suiptifer*, a closely related organism, pulmonary lesions are not infrequent.^{3, 4}

A man with congenital hemolytic jaundice develops chills and fever, paratyphoid B. bacteremia, pyelonephritis, acute cholecystitis, and multiple splenic infarcts.

CASE 2.—A man, 41 years of age, was admitted to the hospital complaining of fever and malaise of five days' duration. He had always been in moderately good health. His illness began suddenly with a chill and pain in the back, headache, malaise and fever. There were no symptoms to indicate the location of the primary infection.

The examination showed a man who had fever, jaundice, enlargement of the liver and spleen, and several large chronic indurated ulcers over the anterior surface of the lower third of the left leg. Laboratory examination showed an anemia; the red blood cell count was 2,230,000, hemo-

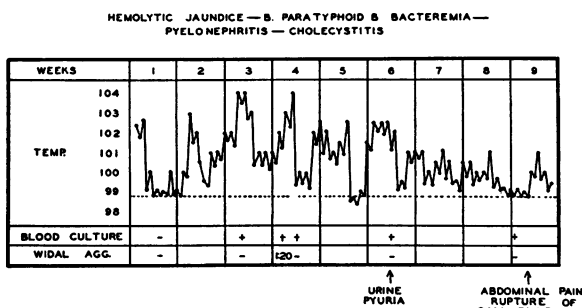


Fig. 2.—(Case 2) Chart showing temperature curve and bacteriologic and serological findings in a patient with hemolytic jaundice and *B. paratyphoid B* bacteremia.

globin 45 per cent, and white blood cell count 5,280. Icteric index was 15 units, bleeding and clotting times were normal, and the reticulocyte count on the day of admission was 0.6 per cent. The stools contained bile pigment. A fragility test showed increased fragility of the red cells characteristic of hemolytic jaundice. The urine was negative except for the presence of a moderately increased amount of urobilinogen. Blood cultures, taken on the third day of entry, were negative. Fig. 2 shows the course of the temperature curve during a period of nine weeks, together with the results of the blood cultures and certain features which appeared during the course of illness.

From the beginning of the third week of illness until the man's death, the blood contained paratyphoid B bacilli on a number of occasions. At the beginning of the sixth week his urine became cloudy and contained numerous leukocytes; and *B. paratyphosus B* was isolated on culture. Several days before death the patient was seized with an acute attack of pain in the upper part of the abdomen, followed by increased rigidity and muscle spasm. He failed rapidly and died nine weeks after admission to the hospital.

The stool cultures were constantly negative for any organisms of the typhoid dysentery group. Widal reaction was carried out, using strains of typhoid bacilli, paratyphoid A and paratyphoid B. On one occasion, two weeks after admission, the Widal was positive, using paratyphoid A, 1-20; but there was no agglutination for paratyphoid B or typhoid bacilli, and no agglutinins appeared in the circulating blood during the entire course of his illness.

The necropsy showed an acute cholecystitis with perforation and generalized peritonitis, splenomegalia with sterile and infected infarcts, multiple abscesses of the kidneys, and jaundice. There were no signs whatsoever of ulceration of the intestines.

From the course of events and the necropsy findings, it would appear that we were dealing with a patient who had hemolytic jaundice and *B. Paratyphosus B* sepsis. The original focus of infection for the bacteremia was not in the gastro-intestinal tract, as might be supposed from finding paratyphoid bacilli in the circulating blood, but they probably arose from the spleen or gall-bladder, and subsequently produced a pyelonephritis. Typhoid or paratyphoid bacilli are found in the circulating blood in the absence of enteric fever when there are foci of infection in other organs, such as the gall-bladder, spleen, or the kidneys; rarely the lungs, bones, or other organs. Many of these infections have been recognized within the past few years as being caused by *B. suipestifer* or paratyphosus C. An excellent review of *B. suipestifer* infection was made recently by Harvey.⁴ Infections of the spleen with this group of organisms had been recorded by Meleney⁵ and Walker and Weiss,⁶ those of the kidney by Morgan,⁷ and those of the gall-bladder by Schottmuller⁸ and others. One interesting feature that stands out in many of these infections,

due to the paratyphoid-suipestifer group, is that they often show up and occur, as in the present case, when there is some chronic illness. Indeed, they occasionally occur as a terminal infection in the course of a disease such as miliary tuberculosis.⁹

The following case illustrates how the positive blood culture gives one an indication concerning the etiology of the underlying infection, in spite of the fact that one may not be able to find decisive evidence for the primary infection.

A man develops chills and fever without localizing signs. Staphylococcus aureus cultured from the blood. Patient dies within seven days after onset, with bilateral bronchopneumonia and acute vegetative endocarditis.

CASE 3.—A man, 52 years of age, was perfectly well until five days before admission to the hospital when he was suddenly seized with a chill and fever and sharp, stabbing pain in the region of the right hip joint. One day later he had another chill with fever, dry unproductive cough, marked prostration, and malaise. His symptoms of prostration increased very markedly within the next few days. Nausea and vomiting became troublesome, as did shortness of breath at rest. His previous histories were non-contributory.

Physical examination showed an acutely ill man who had marked dyspnea. The skin and mucous membranes were dry and showed slight jaundice. Respirations were rapid and shallow and there were numerous, fine, crackling rales at both bases posteriorly. The heart was normal in size and the sounds were clear. There were no murmurs present. The abdomen was negative except for slight tenderness in the costovertebral angle. The extremities were negative. Temperature was 103.6 degrees Fahrenheit, pulse rate 85, and respiratory rate 32. Examination of the urine showed a small amount of albumin, an increase in the number of red cells, a few leukocytes, and an occasional hyaline and granular cast. The red blood cell count was 4,380,000, hemoglobin 85 per cent, and white blood cell count 8,700. X-ray of the chest revealed a diffuse mottling of the lower two-thirds of the right chest and left base. A diagnosis of bronchopneumonia was made. Blood culture on the day of admission showed numerous colonies of *staphylococcus aureus*.

The course of his illness in the hospital was one of progressive failure. The signs of pneumonia increased, blood cultures were positive daily, and on the seventh day of his illness he developed all the signs of peripheral vasomotor collapse, had auricular fibrillation, and died.

The course of this patient's illness, which was extremely rapid, was due to *Staphylococcus aureus* sepsis with bronchopneumonia. The precise diagnosis was not made until the blood cultures were taken. The necropsy showed, in addition to the bronchopneumonia, an acute vegetative endocarditis due to the *Staphylococcus aureus*. In about 10 to 15 per cent of all cases of *Staphylococcus aureus* bacteremia it is not possible to find a focus of entry, and the only way in which a diagnosis can be established is by means of blood cultures. The acute vegetative endocarditis was a finding that was totally unsuspected clinically; but it is in these cases that one not infrequently finds the early stages of bacterial endocarditis due to the *Staphylococcus aureus*.

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(To be continued)

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THE MIDDLE ROAD IN OBSTETRICS AND GYNECOLOGY*

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EVERY now and then it is well for us to pause and reflect upon current trends in medical practice, and upon how we, as individuals, fit into the picture. We, in the field as it were, cannot all be originators of great ideas or procedures, but we may try to be discriminating as to which can be adapted to our own capabilities and temperaments. Fundamental trends in medicine, however, are the products of innumerable minds; we should, therefore, it seems to me, attempt broadly to agree with these until adequate scientific reasons appear for us to do otherwise. But it will always be our problem and duty to conscientiously attempt to distinguish between mere fads and real advance, the while avoiding that overcaution which can stifle progress.

The last several decades have seen a gradual trend toward less surgical and more medical treatment in obstetrics and gynecology. A great fund of endocrine knowledge and theory is accumulating, and manufacturers of endocrines can now supply potent extracts for substitution therapy. Doubtful products of the type offered not so long ago, which were aptly referred to by someone as "slaughterhouse refuse," are disappearing from the market as the demand for properly assayed material increases.

TREND TOWARD CONSERVATISM

The pendulum has been swinging toward a moderate conservatism in gynecologic circles, but there remain a number of men both in and out of the specialty who must be classified as "radical" in their approach to their daily problems. On the other hand, I have seen the work and read publications of others who, in my opinion, are practically hide-bound in their medical outlook. A doctor of this type, in obstetrics particularly, may be blithely following the teachings of the nineteenth century masters of the art, designed as a way out of difficulty in the exigencies of farmhouse practice, in his procedure at the modern, well-equipped maternity.

* Chairman's address, read before the Section on Obstetrics and Gynecology, at the sixty-ninth annual session of the California Medical Association, Coronado, May 6-9, 1940.

Thus the ultraconservative obstetrician becomes, as a matter of fact, the radical, with too frequent unhappy results. Induction of labor at term in normal pregnancy offers a case in point. This procedure has been decried in some quarters as unnecessarily radical, particularly if artificial rupture of membranes is included. In a good hospital, under modern aseptic conditions, with vertex presentation, an adequate pelvis and the cervical canal effaced, I can see no valid objection to its fairly frequent use. Far better, at times, I believe, is this than the head-long rush of the multipara in active labor to the hospital in the family car driven by the distracted husband. Mathieu and Holman have reported a fairly large series of cases with no significant increase in morbidity or mortality of either mother or child. I do not recommend routine employment of induction of labor, but he who categorically condemns it is not making the most of the obstetric art. I feel much the same way about the use of so-called "prophylactic" outlet forceps. Whether or not there is anything prophylactic about it, a woman is frequently saved a lot of work; and if the proper type of forceps is skillfully and gently used, merely to reinforce each labor pain after the head reaches the perineum, no harm, I am convinced, will result. There might even be a lower incidence of extension of the episiotomy wound due to better control.

GYNECOLOGIC ENDOCRINOLOGY

Let us glance again at the subject of gynecologic endocrinology. Here is a great new vista gradually appearing before our eyes, but much, here and there, cannot yet be seen. Work conducted by competent investigators is constantly going on in university laboratories; each year brings new discoveries; but I venture to say that the surface of the subject has as yet only been scratched. The whole story will probably never be known, for therein seems to lie the riddle of life itself, the solution of which Nature will no doubt always contrive to withhold from us. Osler reminded us that, "In seeking absolute truth, we aim at the unattainable and must be content at finding broken portions." This is not the defeatist attitude that it appears to be. One can always strive to apply the knowledge already available in a rational manner. We who are practicing our profession at the bedside and in the office should leave the endocrine experimentation to those who are qualified to conduct it. The indications for the use of almost any endocrine product from whatever manufacturer, as stated in their advertising leaflets, cover practically all of the functional derangements in gynecology. They are fond of parading before us the results of endocrine therapy in rodents and monkeys. No doubt these statements usually agree with the facts, but what is left unsaid is often of more importance to the practitioner. The effect of these products in human beings is often something else again, or they may even be to all intents and purposes inert. The patient who pays high prices for endocrines is entitled to their rational and discriminate use on the part of her doctor, who gains his information on the subject from his well-considered experience and the writings of competent laboratory and clinical observers in the recent medi-